MICROBIOLOGY

بسم الله الرحمن الرحيم

Final | Lecture 1

Vibrios, Campylobacters, Helicobacter

﴿ وَإِن تَتَوَلَّوْا يَسْتَبْدِلْ قَوْمًا غَيْرَكُمْ ثُمَّ لَا يَكُونُوا أَمْثَالَكُم ﴾

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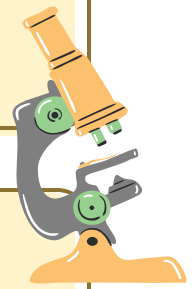

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بسم الله

Vibrios, Campylobacters, Helicobacter and Associated Bacteria

· They are G-ve bacilli, NOT considered as Enterobacteriaceae for 2 reasons:
1- Their different shape (not straight rods).
2- They are oxidase and catalase positive.

By: Nader Alaridah MD, PhD

Overview

Some notes that prof. mentioned are set in other place to match their context.

- They all are motile

- These species are gram-negative rods that are all widely distributed in nature.

- Vibrio cholerae (comma-shaped, with a single polar flagellum), most dramatical cause of watery diarrhea, found in contaminated water, produces an enterotoxin that causes cholera, a profuse watery diarrhea that can rapidly lead to dehydration and death.

- Campylobacter jejuni (S-shape, with single polar flagellum), is a common cause of enteritis, gastroenteritis in humans. It's characterized by bloody diarrhea, found in animal feed & unpasteurized dairy products and undercooked poultry – the most common reservoir.
- Less commonly, Aeromonas and, rarely, Plesiomonas have been associated with diarrheal disease in humans.
- Helicobacter pylori (spiral shape, motile have multiple flagella at one pole) has been associated with peptic ulcers; gastritis and duodenal ulcer disease MALT lymphoma, adenocarcinoma of stomach.

THE VIBRIOS

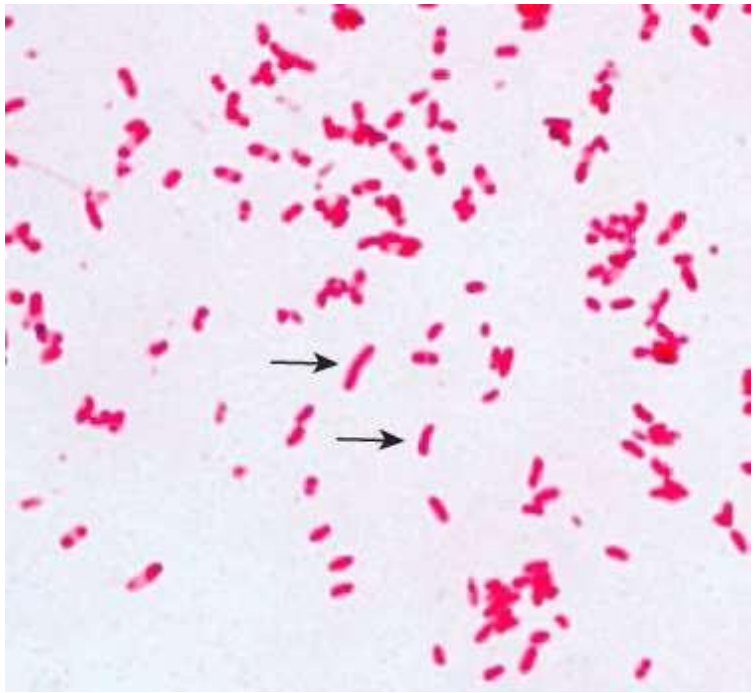
- Vibrios are among the most common bacteria in surface waters worldwide.
- Vibrio cause a number of important infectious syndromes. Classic among them is cholera, a devastating diarrheal disease caused by Vibrio cholerae that has been responsible for seven global pandemics and much suffering over the past two centuries and remains a significant public health concern in the developing world today.
- **V cholerae serogroups O1 and O139 cause cholera in humans.** The O1 serogroup is responsible for six of the seven global pandemics, including the ongoing seventh pandemic, while O139 has caused regional outbreaks. These serogroups are classified based on the structure of the O-specific polysaccharide on the lipopolysaccharide (LPS). Both are associated with pandemic and endemic cholera.[*1(O.A)], and other vibrios may cause soft tissue infections sepsis or enteritis.
- non-O1/non-O139 causes cholera-like disease but is rarely encountered in humans (will be discussed later).

THE VIBRIOS - con.

- Other important Vibrio species that associated primarily with gastrointestinal include **V. parahaemolyticus**, the most common cause of **Sea-foodborne** (**raw fish or shellfish**) **gastroenteritis** in Asia, (they live in water with higher cellularity from surface water that V.cholera O1, O139 live in), and V.vulnificus (oysters), a cause of **severe sepsis** in patients with **cirrhosis** and primary wound infection (Vulnificus is Latin for “wound maker.”) and **V.alginolyticus** occasionally causes eye, ear, and **wound infections**.

VIBRIO CHOLERAE

- The epidemiology of cholera closely parallels the recognition of V cholerae transmission in water, either by drinking contaminated water or using it in cooking, can also be found on the surface of water sources This understanding has driven the development of sanitary water systems.



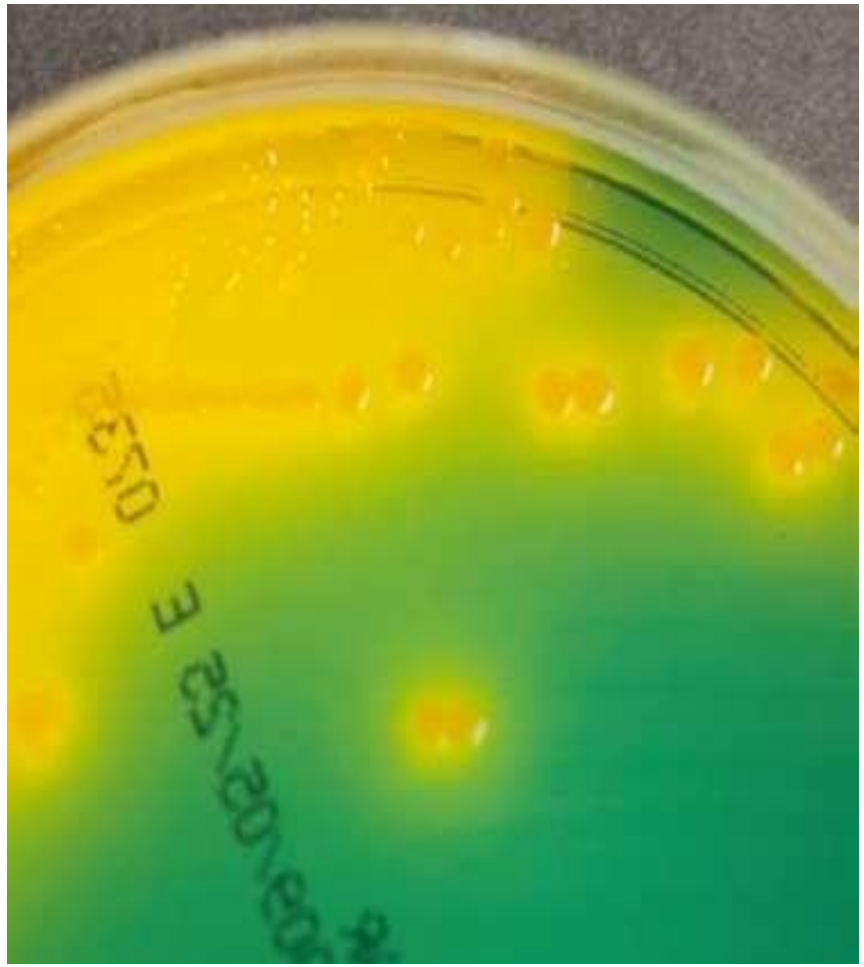
- Vibrio cholerae is found in stagnant or brackish water and can survive in salty marine environments.

- V cholerae is a **comma-shaped**, curved rod 2–4 µm long . It is **actively rapidly motile** (darting motility = sudden movement, it is called: "*shooting star motility*") by means of a polar **flagellum**. On prolonged cultivation, vibrios may become straight rods that resemble the gram-negative enteric bacteria.

- Characteristically, vibrios (O1 & O139) grow at **a very high pH (8.5– 9.5)**,a feature that can be used to aid in their laboratory isolation and are rapidly killed by acid, and are highly sensitive to stomach acidity.

- V cholerae produces **convex, smooth, round colonies** that are opaque and granular in transmitted light.

- V cholera grows well on **thiosulfate-citrate-bile-sucrose (TCBS) agar**, a media **selective** for vibrios, on which it produces **yellow** glistering **colonies** (**sucrose fermented**) that are readily visible against the dark-green background of the agar.



- A **positive oxidase** test result is a key step in the preliminary identification of V. cholerae and other vibrios.

- Vibrio species are susceptible to the compound O/129 (2,4-diamino-6,7-diisopropylpteridine phosphate), which differentiates them from Aeromonas species, which are resistant to O/129.

- Most Vibrio species are **halotolerant,** meaning they can tolerate a certain concentration of NaCl. However, some species, such as V. parahaemolyticus and V. alginolyticus, are halophilic and require a high concentration of NaCl for growth because they naturally inhabit marine environments. In general, the presence of NaCl often stimulates the growth of vibrios.

- Vibrios can multiply up to 3-4 weeks on the surface of stagnated water, and may last longer in present of shellfish.

Antigenic Structure and Biologic Classification

Similar to Enterobacteriaceae antigen

- Many vibrios share a single **heat-labile** flagellar **H** antigen. Antibodies to the H antigen are probably not involved in the protection of susceptible hosts.
- V cholerae has **O** lipopolysaccharides that confer **serologic specificity**. There are at least 206 O antigen groups.
- **V cholerae strains of O group 1 and O group 139 cause classic cholera** (see slide 4 *1(O.A))**; occasionally, non-O1/non-O139 V cholerae causes cholera-like disease.**
- Antibodies to the O antigens tend to protect laboratory animals against infections with V cholerae.
- **Two biotypes of V. cholerae O1, classical and El Tor**, are distinguished. Each biotype is further subdivided into **three serotypes, termed Inaba, Ogawa, and Hikojima.**

Vibrio cholerae Enterotoxin

- **Cholera is a toxin-mediated disease, especially caused by Vibrio cholerae serogroups O1 and O139, which produce cholera toxin (also known as choleragen, encoded by the "CTX genes").**

  - Cholera toxin, a potent protein enterotoxin elaborated by the organism in the small intestine with a molecular weight (MW) of about 84,000, consisting of subunits A (MW,28,000) and B.

  - The genes for V cholerae enterotoxin are on the bacterial **chromosome** **but they are phage transduced (horizontal gene transfer).**

  - **Ganglioside GM1 serves as the mucosal receptor for subunit B** [*2(S.B)], which promotes entry of subunit A into the cell. Activation of subunit A1 yields increased levels of intracellular cyclic adenosine monophosphate **(cAMP)** and results in prolonged **hypersecretion of water and electrolytes.**

Pathogenesis

- Under natural conditions, V cholerae is pathogenic only for humans. A person with normal gastric acidity may have to ingest as many as **10^{10}** or more V cholerae to become infected when the vehicle is water because the organisms are susceptible to acid.
- **When the vehicle is food**, as few as **10^{2}–10^{4}** organisms are necessary **because of the buffering capacity of food** (they prefer alkaline environment).
- The **toxin-coregulated pilus (TCP),** so named because its synthesis is regulated in parallel with that of cholera toxin, is essential for V. cholerae **to survive and multiply in (colonize) the small intestine**.
- Then,"*Choleragen*" is produced, which is composed of **A (active) & B (binding)** subunits. **(see slide 10 *2(S.B))**
- The organisms do not reach the bloodstream but remain within the intestinal tract.
- Virulent V cholerae organisms **attach to the microvilli of the brush border of epithelial cells in the small intestine**. There they multiply and liberate cholera toxin and perhaps mucinases and endotoxin.

Clinical Findings

- The burden of disease is often greatest during “cholera seasons” associated with high temperatures, heavy rainfall, and flooding, but cholera can occur year-round.

- **About 50% of infections with classic V cholerae are asymptomatic, as are about 75% of infections with the El Tor biotype**.

- O139 is milder than O1.

- The incubation period is 12 hours–3 days for persons who develop symptoms, depending largely on the size of the inoculum ingested.

- There is a **sudden onset** of nausea and vomiting and **profuse** watery **diarrhea (Most dramatical diarrhea)** with abdominal cramps. Stools, which resemble **“rice water”**, **contain mucus, epithelial cells, and large numbers of vibrios.**

- There is a rapid loss of fluid and electrolytes, which leads to **profound dehydration**, circulatory collapse, and anuria. **The mortality rate without treatment is between 25% and 50%,** because the patient may suffer from hypovolemic shock.

- The diagnosis of a full blown case of cholera presents no problem in the presence of an epidemic. However, sporadic or mild cases are not readily differentiated from other diarrheal diseases. The El Tor biotype tends to cause milder disease than the classic biotype.

Diagnostic Laboratory Tests

A. Specimens:

- Specimens for culture consist of **mucus flecks from stools**.

B. Smears:

- **Dark-field or phase contrast microscopy** may show the **rapidly motile vibrios**.

C. Culture:

- Growth is rapid in peptone agar, on blood agar with a pH near 9.0, or on TCBS agar, and typical colonies can be picked in 18 hours.

D. Specific Tests:

- V cholerae organisms are further identified by slide **agglutination tests** using **anti-O group 1 or group 139** antisera and by biochemical reaction patterns

(immunochromatographic dipstick assays: very rapid -antigen- test for O1 & O139).

- Alkaline enrichment culture may be used.

Treatment

- The most important part of therapy consists of water and electrolyte replacement to correct the severe dehydration and salt depletion.

- Many antimicrobial agents are effective against V cholerae, but these play a secondary role in patient management. Oral tetracycline and doxycycline tend to reduce stool output in cholera and shorten the period of excretion of vibrios.

- In some endemic areas, tetracycline resistance of V cholerae has emerged; the genes are carried by transmissible plasmids. In children and pregnant women, alternatives to the tetracyclines include erythromycin and furazolidine .
  - **Tetracyclines are contraindicated in children and pregnant women**; messes with teeth and bone development.

Prevention

❖ Provision of safe water and of facilities for sanitary disposal of feces, improved nutrition, and attention to food preparation and storage in the household can significantly reduce the incidence of cholera.

· People infected with the **O1 or O139** serotypes develop **partial**, **serotype-specific immunity**, which typically **lasts two to three years at most.**

❖ Currently, two oral killed cholera vaccines have been prequalified by the WHO and are available internationally:

- WC-rBS (Dukoral.; Crucell, Stockholm, Sweden) contains several biotypes and serotypes of V. cholerae O1 supplemented with recombinant cholera toxin B subunit.
- BivWC (Shanchol™; Shantha Biotechnics–Sanofi Pasteur, Mumbai, India) contains several biotypes and serotypes of V. cholerae O1 and V. cholerae O139 without supplemental cholera toxin B subunit.

· There are **three** vaccines for V. cholera. However, none of them are a part of the national vaccination program due to their moderate efficacy (~50%) and short immunity.

WC: whole cell

CAMPYLOBACTER

- Campylobacters are motile, non-spore-forming, curved, gram-negative rods.
- Campylobacters are found in the gastrointestinal tract of many animals used for food (including poultry, cattle, sheep, and swine) and many household pets (including birds, dogs, and cats)
- Campylobacters cause both diarrheal and systemic diseases and are among the most widespread causes of infection in the world.
- The classification of bacteria within the family Campylobacteriaceae has changed frequently. Some species previously classified as campylobacters have been reclassified in the genus Helicobacter. The genus Arcobacter has been created.
- The human pathogens fall into two major groups: those that primarily cause diarrheal disease and those that cause extraintestinal infection
  - An infected puppy with diarrhea can transmit Campylobacter to household members through direct contact.
  - The most common cause of gastroenteritis is **viruses.**
  - The most common cause of **bacterial gastroenteritis** in the developed world: **Campylobacter** > **Salmonella** > **Shigella**.

- Campylobacter jejuni is the prototype organism in the group and is a very common cause of diarrhea in humans.

- Campylobacter fetus has two subspecies, fetus and venerealis. C fetus subspecies fetus is an opportunistic pathogen that causes systemic infections in immunocompromised patients. It may occasionally cause diarrhea.

- Other organisms that cause diarrheal disease include Campylobacter coli, Campylobacter upsaliensis (dogs), Campylobacter lari (seagulls), Campylobacter hyointestinalis, Campylobacter fetus, Arcobacter butzleri, Arcobacter cryaerophilus, Helicobacter cinaedi, and Helicobacter fennelliae.

  - Nota bene: These species of **Arcobacter & Helicobacter** are a part of the **Campylobacter family**. They cause gastrointestinal disease and are infrequent causes of human disease.

Campylobacter Species

Campylobacters can cause gastroenteritis, enterocolitis, and extraintestinal infections.

1) Campylobacter jejuni: affects the jejunum

2) Campylobacter coli: affects the large bowel

3) Campylobacter fetus: mainly causes extraintestinal diseases, bacteremia, soft tissue, and nosocomial infections, especially in immunocompromised patients. It may cause gastroenteritis as well.

CAMPYLOBACTER JEJUNI AND CAMPYLOBACTER COLI

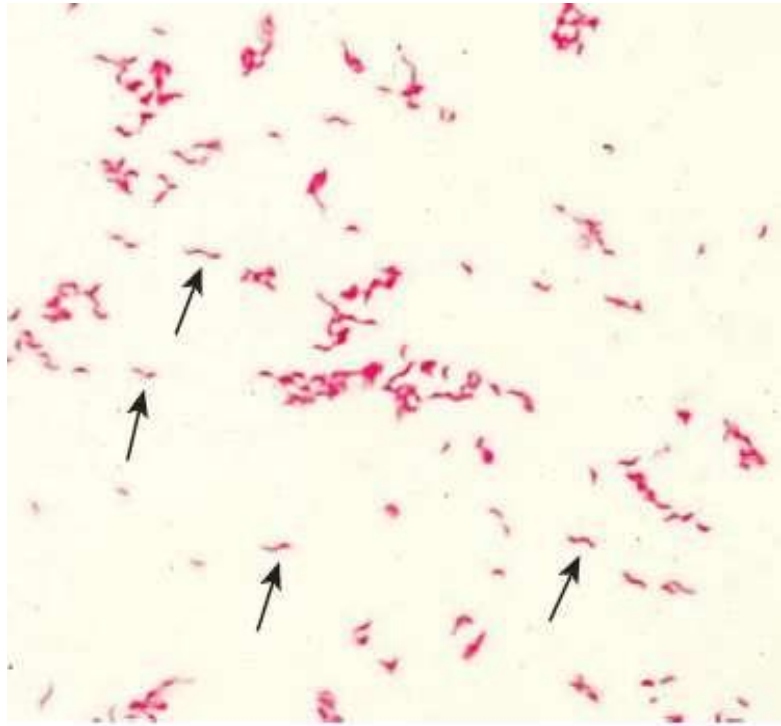
- C jejuni and Campylobacter coli have emerged as common human pathogens, causing mainly enteritis and occasionally systemic infection.

- C jejuni and C coli cause infections that are clinically indistinguishable, and laboratories generally do not differentiate between the two species.

- Between 5% and 10% of infections reported to be caused by C jejuni are probably caused by C coli. These bacteria are at least as common as salmonellae and shigellae as a cause of diarrhea especially in the developed world.

CAMPYLOBACTER JEJUNI

- gram-negative rods with comma, S, or "**gull wing**" shapes. They are motile, with a single polar flagellum, and do not form spores.



- Selective media are needed, and incubation must be in an atmosphere with reduced O2 (5% O2) with added CO2 (10% CO2).

- Incubation of primary plates for isolation of C jejuni should be at 42°C. Although C jejuni grows well at 36–37°C, incubation at 42°C prevents growth of most of the other bacteria present in feces, thus simplifying the identification of C jejuni. Several selective media are in widespread use.

Campylobacter jejuni

While Vibrio cholera appears comma-shaped, Campylobacter jejuni exhibits a seagull-wing appearance, or S-shape characteristic under the microscope. It is also motile as it has a polar flagellum, which enables its unique **corkscrew-like** motion.

They are thermophilic (42º C) and microaerophilic bacteria.

Pathogenesis

- The infection is acquired by the oral route from food, drink, or contact with infected animals or animal products, especially poultry.
- C jejuni is susceptible to gastric acid, and ingestion of about 10^4 organisms is usually necessary to produce infection.
- Both the motility of the strain and its capacity to adhere to host tissues appear to favor disease, but classic enterotoxins and cytotoxins (cytolethal distending toxin, or CDT) appear not to play substantial roles in tissue injury or disease production.
- The organisms multiply in the small intestine, invade the epithelium (more specifically, **Peyer's patches**), and produce inflammation that results in the appearance of red and white blood cells in the stools. Occasionally, the bloodstream is invaded, and a clinical picture similar to enteric fever develops. Localized tissue invasion coupled with the toxic activity appears to be responsible for the enteritis.
  - **CDT's mechanism of action is not fully understood.**

Clinical Findings

- A prodrome of fever, headache, myalgia, and/or malaise often occurs 12–48 h before the onset of diarrheal symptoms. profuse diarrhea that may be grossly bloody.
- Usually the illness is self-limited to a period of 5–8 days, but occasionally it continues longer.
- Most cases resolve without antimicrobial therapy; however, in about 5–10% of patients, symptoms may recur.
- Local suppurative complications of infection include cholecystitis, pancreatitis, and cystitis; distant complications include meningitis, endocarditis, arthritis, peritonitis, cellulitis, and septic abortion. All these complications are rare, except in immunocompromised hosts
- Hepatitis, interstitial nephritis, and the hemolytic-uremic syndrome occasionally complicate acute infection
- Certain serotypes of C jejuni have been associated with post-diarrheal Guillain-Barré syndrome, a form of ascending paralytic disease. Reactive arthritis and Reiter's syndrome may also follow acute campylobacter diarrhea.

Campylobacter fetus

- Patients infected with ***Campylobacter jejuni*** typically present with an initial phase of **watery diarrhea** that **may progress to bloody diarrhea** due to mucosal inflammation. While ***C. jejuni*** and ***C. coli*** primarily cause gastrointestinal illness, they can also invade the walls of the **jejunum** and **colon**, occasionally spreading **locally** within the abdomen (causing peritonitis) or even to distant organs, leading to rare complications such as **meningitis**, **endocarditis**, or **septic arthritis**, which may occur post-Campylobacter infection. In contrast, *Campylobacter fetus* is more likely to cause **systemic infection**, such as **bacteremia**, because it invades **both** the mucosa and submucosa, gaining **direct access to the bloodstream**.

Guillain-Barré Syndrome

- An autoimmune disease where the immune system attacks the peripheral nerves causing muscle weakness and **ascending flaccid paralysis** (in contrast to the descending paralysis caused by C. botulinum). Infections with the **O19 serotype** of **Campylobacter jejuni** can trigger Guillain-Barre. This bacterium expresses **LOS** (**lipooligosaccharides**) that **mimic gangliosides** on neuronal cells. The host immune system produces **anti-LOS** antibodies, which cross-react with the gangliosides present in the neuronal cells. This causes immune-mediated neuropathy commonly following **gastroenteritis** caused by Campylobacter.

○ One-sentence summary: Campylobacter O19 LOS look like our own neuronal cells, so when our immune system produces antibodies to fight off the bacteria, it attacks our neuronal cells, thinking they are bacteria due to molecular mimicry.

Diagnostic Laboratory Tests

- A. Specimens
- Diarrheal stool is the usual specimen. C jejuni , C fetus , and other campylobacters may occasionally be recovered from blood cultures usually from immunocompromised or elderly patients.
- B. Smears
- Gram-stained smears of stool may show the typical “**gull wing**”–shaped rods. Dark-field or phase contrast microscopy may show the typical **darting motility** of the organisms.
- C. Culture
- Culture on the selective media (Skirrow's, Butzler's, Blaser's, Campy-BAP and Preston media) is the definitive test to diagnose C jejuni enteritis. If another species of Campylobacter is suspected, medium without a cephalosporin should be used and incubated at 36–37° C.

Treatment

- Fluid and electrolyte replacement is central to the treatment of diarrheal illnesses.
- Even among patients presenting for medical attention with Campylobacter enteritis, not all clearly benefit from specific antimicrobial therapy. Indications for therapy include high fever, bloody diarrhea, severe diarrhea, persistence for >1 week, and worsening of symptoms. A 5- to 7-day course of erythromycin is the regimen of choice.
- An alternative regimen for adults is ciprofloxacin or another fluoroquinolone for 5–7 days. - Alternative for patients who are allergic to erythromycin or when it is contraindicated.
- For systemic infections, treatment with gentamicin or imipenem or chloramphenicol should be started empirically, but susceptibility testing should then be performed

  ○ Campylobacter fetus can be found in the genital tract and, thus, another route of transmission (besides fecal-oral) is through **vertical transmission** (mother to fetus). These cases should have **gentamicin** or **Chloramphenicol** prescribed to them for treatment.

HELICOBACTER PYLORI

- In Arabic, H. pylori is called الجرثومة الحلزونية

- H pylori is **a spiral-shaped** gram-negative rod.
- It has **multiple flagella** at one pole and is actively motile.
- The organism has several acid-resistance mechanisms, most notably a highly expressed **urease** that catalyzes urea hydrolysis to produce buffering ammonia. H. pylori is microaerophilic (i.e., requires low levels of oxygen), is oxidase positive and catalase positive is slow-growing, and requires complex growth media in vitro.

○ Takes about 8-10 days to start growing. It can be cultured on specialized media such as **Skirrow's agar**, **Campy-BAP**, **chocolate agar**, **brain heart infusion.** Growth requires complex nutrients and microaerophilic conditions, which are not part of routine laboratory culture protocols.

- H pylori is associated with antral gastritis, duodenal (peptic) ulcer disease, gastric ulcers, gastric adenocarcinoma and gastric mucosa-associated lymphoid tissue (MALT) lymphomas. It may be one initial precipitant of pernicious anemia and also may predispose some patients to iron deficiency through occult (hidden) blood loss and/or hypochlorhydria and reduced iron absorption.

○ H. pylori has been classified by the WHO as a Group I carcinogen, linked to a lifetime risk of **gastric adenocarcinoma** or **B-cell lymphoma**. It's responsible for ~90% of duodenal ulcers and ~85% of gastric ulcers. **NSAID** use is the second cause of peptic ulcers following H. pylori.

Epidemiology

- Helicobacter pylori colonizes the stomach in ~50% of the world's human population, essentially for life unless eradicated by antibiotic treatment.
- Humans are the only important reservoir of H. pylori. Children may acquire the organism from their parents (most often the primary caregiver) or from other children.
- Most H. pylori–colonized persons do not develop clinical sequelae. That some persons develop overt disease whereas others do not is related to a combination of factors: bacterial strain differences (cag-positive , type IV secretion system, the vacuolating cytotoxin VacA), host susceptibility to disease, and environmental factors (the interleukin 1 gene polymorphisms, and smoking).

  ○ The absence of these factors does not guarantee that H. Pylori colonization will not progress to invasion and infection; rather, their presence increases the likelihood of disease progression.

Epidemiology

· Incidence of *H. Pylori is* significantly **higher** in developing countries compared to developed countries. Some studies estimate that over 2/3 of the global population is colonized by *H. pylori.*

· **Streptococcus**, **Haemophilus**, and **Providentia** are **all inhabitants** of the stomach, a part of the gut microbiome, but they're **not pathogenic** microorganisms. **In contrast**, *H. pylori* is the main pathogenic microorganism associated with the stomach.

· The transmission routes include fecal-oral and oral-oral, and it is common for family members (e.g., parents and siblings) to be infected.

· **Colonization → infection → inflammation** → disease (**ulcer**, **MALT lymphoma**, **gastric adenocarcinoma**).

· Immunocompromised individuals (e.g., those with HIV or cancer) are more likely to develop disease, as impaired immunity allows easier progression from colonization to invasive infection.

·Patients with **interleukin-1** receptor gene polymorphisms are especially predisposed to severe ***H. pylori***-associated diseases due to heightened inflammatory responses.

Pathogenesis

- There is No set pathogenesis, but a cluster of factors instead.

- H pylori is found deep in the mucous layer near the epithelial surface where physiologic pH is present.

- H pylori is quite motile(Corkscrew movement) even in mucus, and is able to find its way to the epithelial surface. H pylori overlies gastric-type but not intestinal- type epithelial cells.

- H. pylori "swim" to the gastric epithelial lining, where the pH is higher than the lumen, as a protective mechanism.

- H pylori also produces a protease that modifies the gastric mucus and further reduces the ability of acid to diffuse through the mucus.

  - Hiding in the mucus membranes due to having mucinases.
  - The presence of cytotoxins results in the cytotoxicity of gastric types of epithelial cells.

- H pylori produces potent urease activity, which yields production of ammonia and further buffering of acid.

- The mechanisms by which H pylori causes mucosal inflammation and damage are not well defined but probably involve both bacterial and host factors.

- The bacteria invade the epithelial cell surface to a limited degree.

- Toxins and lipopolysaccharide may damage the mucosal cells, and the ammonia produced by the urease activity may also directly damage the cells.

- Polymorphonuclear and mononuclear cell infiltrates are seen within the epithelium and lamina propria. Vacuoles within cells are often pronounced.

Destruction of the epithelium is common, and glandular atrophy may occur.

- The primary phenomena after H.pylori colonization and infection:
After taking a biopsy from a patient, histopathologists confirm the presence of gastritis due to the recruitment of inflammatory cells (mononuclear or polymorphic) and may add whether H.pylori seen or not.

- H pylori thus is a major risk factor for gastric cancer.

H. pylori colonization induces chronic superficial gastritis, a tissue response in the stomach that includes infiltration of the mucosa by both mononuclear and polymorphonuclear cells.

· Acute or chronic gastritis can be the first step in multi step process (metaplasia).
Where the gastric type cells after death are replaced by intestinal type cells which can end up with cancer.

Clinical Findings

- Acute infection can yield an upper gastrointestinal illness with nausea and epigastric pain; vomiting, acid regurgitation and fever may also be present. (Fever is very rare with peptic ulcer)

- The acute symptoms may last for less than 1 week or as long as 2 weeks.

- After colonization, the H pylori infection persists for years and perhaps decades or even a lifetime.

- About 90% of patients with duodenal ulcers and 50–80% of those with gastric ulcers have H pylori infection.

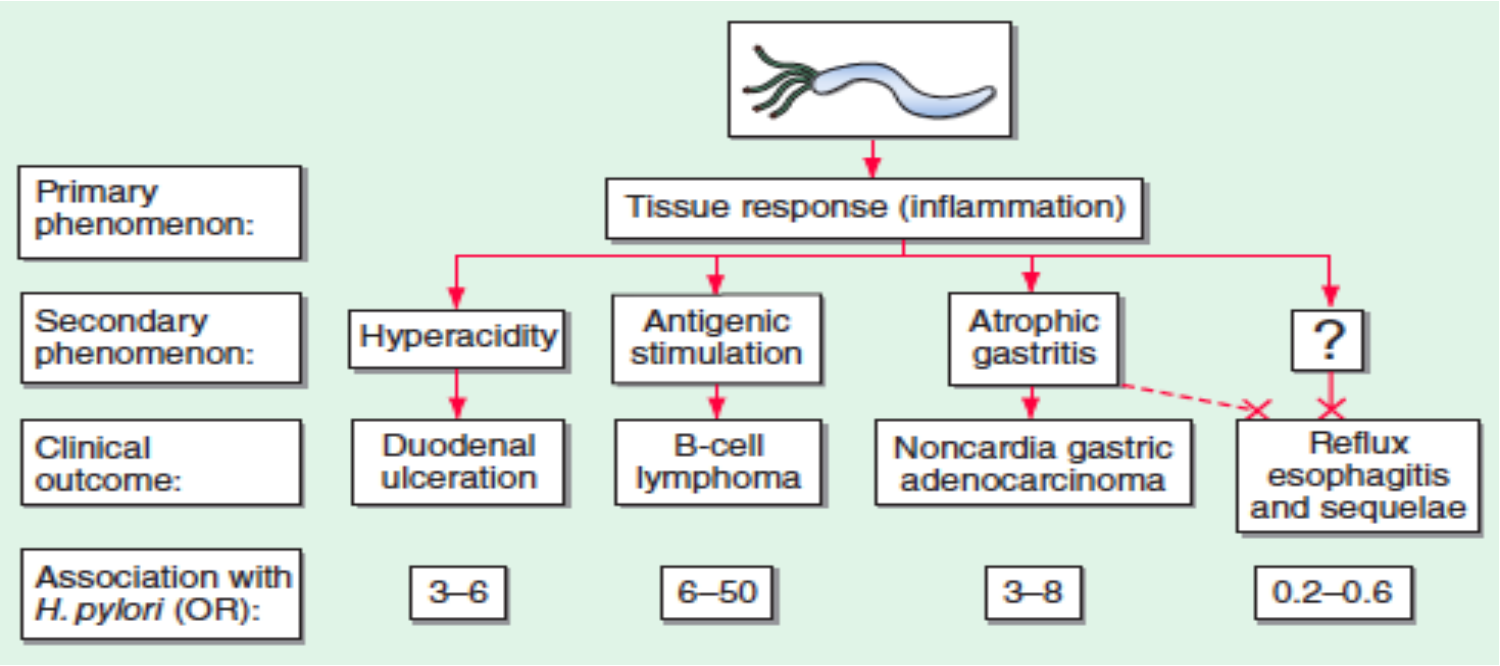
- Recent studies confirm that H pylori also is a risk factor for gastric carcinoma and lymphoma.

Relationships between colonization with Helicobacter pylori and diseases of the upper gastrointestinal tract.

In statistics, odd ratio measures the relation between the exposure of a certain stimuli and the outcome of it.

Odd ratio > 1 positive association علاقة طردية

Odd ratio < 1 negative association علاقة عكسية



OR>1 علاقة طردية

· Most patients who develop colonization of H. pylori to infection, they form a **tissue response** in the form of acute or chronic gastritis, mainly (recruitment of inflammatory cells).

· As a secondary phenomenon, some people may develop duodenal ulcers
*Note how many folds increase (3-6 times).

· Continuous antigenic stimulation by H. pylori antigen might result in B-cell lymphoma as well as adenocarcinoma of the stomach.

OR<1 علاقة عكسية* (Patients infected with H. pylori are less likely to develop these conditions)

· GERD (gastroesophageal reflux)
· Adenocarcinoma of the oesophagus.

Pan gastritis: inflammation of the entire stomach

Diagnostic Laboratory Tests

❖ Smears

- The diagnosis of gastritis and H pylori infection can be made histologically. A gastroscopy procedure with biopsy is required. Routine stains demonstrate gastritis, and Giemsa or special silver stains can show the curved or spiral-shaped organisms.

○ If it was not seen, it does not mean that it is not present, because it depends on the biopsy site (most commonly, the biopsy is taken from the gastric antrum, where we have few parietal cells), but
the infection can be at the lesser or greater curvature, or it can be pan gastritis..

❖ Culture

- Culture is performed when patients are not responding to treatment, and there is a need to assess susceptibility patterns.

○ **Not stool culture, biopsy culture**
Homogenization -> culture on brain heart or chocolate agar.
There is a very complex growth supplement for Helicobacter; they need 1 week on the agar to be seen.

Diagnostic Laboratory Tests

❖ Special Tests (Invasive technique)

- Rapid tests to detect urease activity in vitro are widely used for presumptive identification of H pylori in specimens.

  5-6 biopsies -> histopathology -> microbiology lab -> addition of urea -> detection of urease activity; If it is present, bubbles will appear on the tissue sample.

- In vivo tests for urease activity can be done also. In urea breath tests, 13 C- or 14 C- labeled urea is ingested by the patient. If H pylori is present, the urease activity generates labeled CO2 that can be detected in the patient's exhaled breath.

  ○ We ask the patient to swallow isolated carbon-labelled urea. If H. pylori is present, then there will be urease activity; urea is split into ammonia and CO2.

- Detection of H pylori antigen in stool specimens is appropriate as a test of cure for patients with known H pylori infection who have been treated.

- It is used mainly to follow up treatment, but it can be used for diagnosis.

Treatment

- **Triple therapy** with metronidazole and either bismuth subsalicylate or bismuth subcitrate plus either amoxicillin or tetracycline for 14 days eradicates H pylori infection in 70–95% of patients.

○ In our countries, these percentages are not totally true; many individuals were unable to eradicate H. pylori. This may be due to decreased sensitivity, as many children receive amoxicillin frequently.
○ Diet and other environmental factors play an indirect role and are considered confounders.
- Adenocarcinoma is not seen as much as gastric ulcer in Jordan, whereas in China it is significantly seen due to differences in diet.

- An acid-suppressing agent given for 4 o 6 weeks enhances ulcer healing. Proton pump inhibitors (PPIs) directly inhibit H pylori and appear to be potent urease inhibitors.

- The preferred initial therapy is 7–10 days of a PPI plus amoxicillin and clarithromycin or a **quadruple regimen** of a PPI metronidazole, tetracycline, and bismuth for 10 days.

PLESIOMONAS

Not Required

- Un-commonly, Plesiomonas have been associated with diarrheal disease in humans.
- Plesiomonas shigelloides is an oxidase positive, gram-negative rod with polar flagella.
- Plesiomonas is most common in tropical and subtropical areas. It is a water and soil organism and has been isolated from freshwater fish and many animals.
- Most isolates from humans have been from stool cultures of patients with diarrhea.
- Plesiomonas grows on the differential media used to isolate Salmonella and Shigella from stool specimens .
- Some Plesiomonas strains share antigens with Shigella sonnei, and cross-reactions with Shigella antisera occur. Plesiomonas can be distinguished from shigellae in diarrheal stools by the oxidase test: Plesiomonas is oxidase positive, and shigellae are not.
- Plesiomonas species are positive for DNase; this and other biochemical tests distinguish it from Aeromonas species.

Not Required

Aeromonas

- Aeromonas species are distinguished from the enteric gram-negative rods by finding a positive oxidase reaction in growth obtained from a blood agar plate. Aeromonas species are differentiated from vibrios by showing resistance to the compound O/129 and lack of on media containing 6% NaCl.
- Typically, aeromonads produce hemolysins. Some strains produce an enterotoxin, Cytotoxins and the ability to invade cells in tissue culture have been noted.
- However, gastroenteritis, caused mostly by A caviae complex, ranges from acute watery diarrhea to less commonly a dysenteric type of illness.
- Aeromonas species are also associated with extraintestinal infections such as bacteremia and wound infections. The latter are often the result of trauma that occurs in a water environment and are caused primarily by A hydrophila

Not Required

Treatment

- Aeromonas and Plesiomonas species are generally susceptible to fluoroquinolones (e.g., ciprofloxacin), third- and fourth-generation cephalosporins carbapenems, and aminoglycosides, but resistance has been described to all those agents. Because Aeromonas can produce various β-lactamases, including carbapenemases,
- Susceptibility testing must be used to guide therapy.

The End

For any feedback, scan the code or click on it.

Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1	Slide 9 Slide 11	(see slide 7 *1(O.A)) (see slide 13 *2(S.B))	(see slide 4 *1(O.A)) (see slide 10 *2(S.B))
V1 → V2	Slide 37	Campylobacter	Helicobacter

Additional Resources:

Extra References for the Reader to Use:

1. Campylobacter jejuni- Sketchy
2. Campylobacter jejuni- Physeo
3. Vibrio cholera & vulnificus- Physeo
4. Helicobacter pylori- Physeo
5. There are Sketchy videos for Vibrio & Helicobacter pylori on this Telegram channel.

Embrace the moment and clear your mind as the sun sets.

رسالة من الفريق العلمي:

فعن عبدالله –يعني: ابن مسعود رضي الله عنه وأرضاه- قال: قال رسولُ الله ﷺ: ما أصاب أحدًا قطُّ همٌّ ولا حزنٌ فقال: اللهم إني عبدك، ابن عبدك، ابن أمتك، ناصيتي بيدك، ماضٍ فيَّ حكمك، عدلٌ فيَّ قضاؤك، أسألك بكل اسمٍ هو لك، سميتَ به نفسَك، أو علَّمتَه أحدًا من خلقك، أو أنزلتَه في كتابك، أو استأثرتَ به في علم الغيب عندك؛ أن تجعل القرآنَ ربيع قلبي، ونور صدري، وجلاء حزني، وذهاب همّي؛ إلا أذهب اللهُ همَّه وحُزنَه، وأبدله مكانه فرحًا، قال: فقيل: يا رسول الله، ألا نتعلَّمها؟ فقال: بلى، ينبغي لمن سمعها أن يتعلَّمها.

اللهم لا تحقق لأعدائك غاية ولا ترفع لهم راية واللهم من أراد بالمسلمين سوءًا أبطنه فاكشف عنه سترك.